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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------------------|-----------------------------|
| 10/594,163 | 09/26/2006 | Kenichi Koyakumaru | 701062 | 7239 |
| 23460 7590 12/14/2009 LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6731 | | | EXAMINER CLARK, SARA E | |
| | | | ART UNIT 1612 | PAPER NUMBER |
| | | | NOTIFICATION DATE 12/14/2009 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 7/15/2009.

Claims 1 and 7 have been amended.

No new claims have been added.

Thus, claims 1-24 now represent all claims currently pending and under consideration.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement (IDS) submitted on 7/15/2009 was filed after the mailing date of the first action on the merits on 3/17/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

WITHDRAWN OBJECTIONS/REJECTIONS

Objections

Applicant's arguments, see Remarks, pp. 7-8, filed 7/15/2009, with respect to the objections to the specification and claims 1-24, have been fully considered and are persuasive. Therefore, the objections have been withdrawn.

Double Patenting Rejections

Applicant's arguments, see Remarks, pp. 12-13, filed 7/15/2009, with respect to the obviousness-type double patenting rejection of instant claims 1-24 over claims 7, 8, and 13-18 of copending application 10/594,164 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

The terminal disclaimer filed on 7/15/2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on co-pending application 10/594,164 has been reviewed and is accepted. The terminal disclaimer has been approved and recorded.

MAINTAINED REJECTIONS

Rejections under 35 USC §103(a)

Claims 1-24 stand rejected under 35 USC §103(a) as obvious over Nakazawa et al. (US Pub. 2003/0181742) in view of Moriarty et al. (Tetrahedron Let. 35(44) 8103-6, 1994). See below.

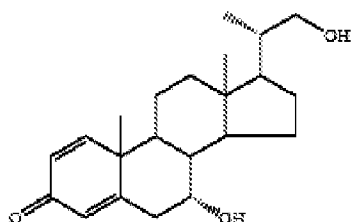
RESPONSE TO ARGUMENTS

The examiner's understanding of the inventive concept of the claimed invention is protection of the 21-hydroxyl group, the 7-hydroxyl group, or both, to suppress side reactions and decrease degradation of the catalyst, thereby decreasing the amount of catalyst required while increasing the yield. The examiner also agrees with Applicant's

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assertion that a Birch reduction (metal lithium in ammonia) does not necessarily require protection of hydroxyl groups prior to the Birch reduction step; indeed, an unprotected hydroxyl group can aid the reaction by serving as a proton donor (see Remarks, p. 10, first paragraph; and p. 11, third paragraph).

To summarize, Nakazawa et al. teach the use of lithium in a Birch reduction of the C₁-C₂ and C₄-C₅ double bonds of the unprotected compound corresponding to the claimed reactant of formula (I) (formula I-1, para. 0020),

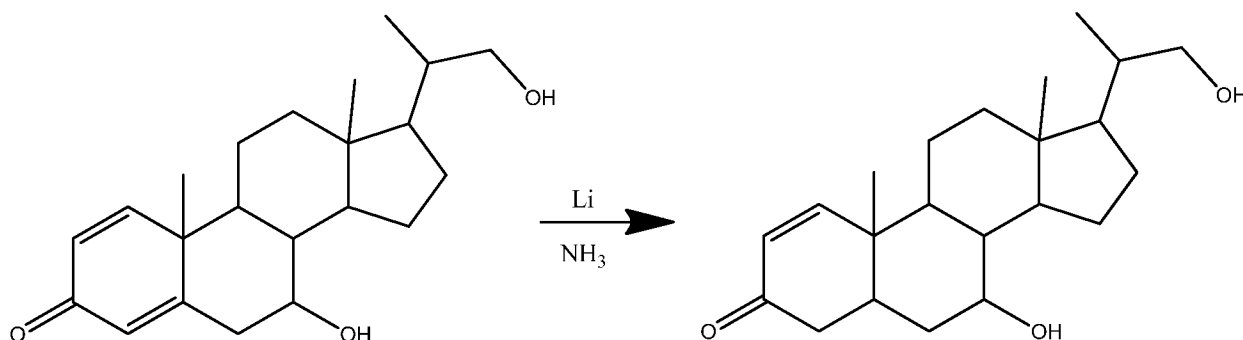


in amounts which overlap the claimed range (para. 0050, where “gram-atom” is understood as an obsolete term equivalent to “mole”):

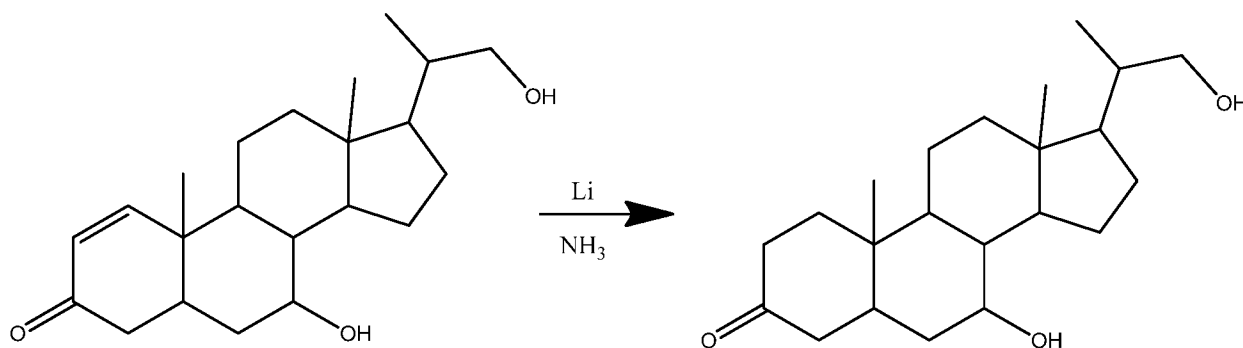
Examples of the alkali metal usable for the above purpose are lithium, sodium, potassium and rubidium; and those of the alkali earth metals are calcium, strontium and barium. These alkali metals or alkali earth metals may be used desirably in an amount of **at least 2 gram atoms based on 1 mole of the compound (I)**, more preferably in a range of 2 to 20 gram atoms on the same basis.

Further, Applicant's finding that the C₄-C₅ double bond is more easily reduced than the C₁-C₂ double bond would be expected by one of ordinary skill in the art, because the C₁-C₂ double bond is more sterically hindered due to the C₁₀ methyl group, giving the reducing agent better access to the C₄-C₅ double bond, which would therefore be predicted to react more readily.

In addition, it was noted in the Office Action dated 3/17/2009 that this mechanism is inherent in the method of Nakazawa et al. Applicants contend that the intermediate 1-ene-3-one would not ultimately be produced (Remarks, p. 9, third paragraph). However, it would be produced as an intermediate as the reaction proceeds: because the C₄-C₅ double bond is less sterically hindered and more susceptible to reduction, it would be expected to be reduced first, in the initial phase of the reaction:



As the reaction proceeds, the more sterically hindered and less susceptible C₁-C₂ double bond would then be reduced:

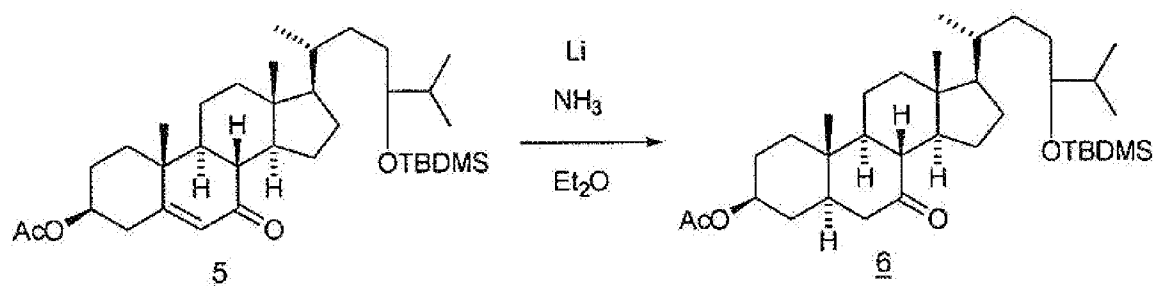


Therefore, Nakazawa et al. explicitly and inherently disclose the claimed process using the 7,21-unprotected species of the claimed compounds. Nakazawa et al. do not

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teach protection of the 21-hydroxyl group prior to the Birch reduction step, followed by deprotection.

However, Moriarty et al. teach protection of a 24-hydroxyl group with the claimed hydroxyl-protecting group prior to a Birch reduction, as shown in the figure provided by Applicants (Remarks, p. 10),



Applicant argues that Moriarty does not provide a credible reason for one of ordinary skill in the art to protect hydroxyl group prior to a Birch reduction (see Remarks, p. 11, third paragraph). However, Moriarty does not have to provide a reason for protecting a hydroxyl group before a Birch reduction. The issue here is whether the skilled artisan would have a reasonable expectation that the claimed reaction would run in the presence of hydroxyl protecting group. The reaction above is evidence that the skilled artisan would reasonably expect the Birch reduction to proceed in the presence of a t-butyl-dimethylsilyl hydroxyl-protecting group, regardless of the reasons contemplated by Moriarty et al. for introducing it. The reference teaches that protecting a hydroxyl group prior to a Birch reduction would not adversely affect the reaction.

Because a Birch reduction using Li/NH₃ was known to proceed successfully in either the presence or absence of hydroxyl protecting groups, one of ordinary skill in the

art would have been motivated to modify the compounds of Nakazawa et al. by protecting the 21-hydroxyl group prior to the Birch reduction step with a reasonable expectation of success. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (BPAI 1985).

NEW REJECTIONS

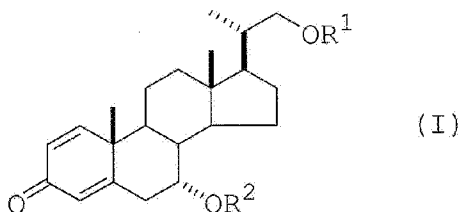
Claim Rejections - 35 USC § 112, Second Paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 1-24 have been amended to limit the alkali or alkaline earth metal present in the reaction to “an amount of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions” of formula (I).



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However, the amount necessary to reduce the C₄-C₅ double bond is not disclosed or otherwise readily discerned. The specification (p. 14, line 31 to p. 15, line 10) discloses only that

The amount of these alkali metal or alkaline earth metal to be used is not particularly limited as long as the reduction of the carbon-carbon double bond at the 4,5-positions of compound (I) is almost completed and the carbon-carbon double bond at the 1,2-positions of compound (I) can partly remain. However, in order to significantly suppress the reduction of ketone, **the amount is generally within the range of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions of compound (I).** When the amount of alkali metal or alkaline earth metal to be used is less than such range, reduction of the carbon-carbon double bond at the 4,5-positions of compound (I) tends not to be completed, and when it is greater than such range, side reactions (e.g., reduction of ketone and the like) tend to proceed.

Because the amount of the alkali or alkaline earth metal to be used is defined only in relative rather than absolute terms, that is, relative to an undisclosed quantity, and not in any specific, definite way, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 112, First Paragraph

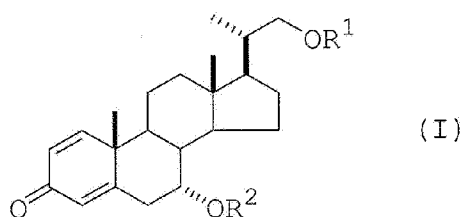
Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, claims 1-24 have been amended to limit the alkali or alkaline earth metal present in the reaction to “an amount of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions” of formula (I).



However, the amount necessary to reduce the C₄-C₅ double bond is not disclosed or otherwise readily determined. The specification (p. 14, line 31 to p. 15, line 10) discloses only that

The amount of these alkali metal or alkaline earth metal to be used is not particularly limited as long as the reduction of the carbon-carbon double bond at the 4,5-positions of compound (I) is almost completed and the carbon-carbon double bond at the 1,2-positions of compound (I) can partly remain. However, in order to significantly suppress the reduction of ketone, **the amount is generally within the range of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions of compound (I).** When the amount of alkali metal or alkaline earth metal to be used is less than such range, reduction of the carbon-carbon double bond at the 4,5-positions of compound (I) tends not to be completed, and when it is greater than such range, side reactions (e.g., reduction of ketone and the like) tend to proceed.

The amount of the alkali or alkaline earth metal to be used is defined only in relative rather than absolute terms, that is, relative to an undisclosed quantity, and not in any specific, definite way.

To illustrate, the only example provided in the disclosure (Example 1, p. 23, lines 22-28) uses 46.1 mmol lithium in the partial reduction of 10.9 mmol of the diene reactant; that is, to reduce formula (I) to a mixture of the unsaturated product of formula (II) and the mono-unsaturated product of formula (III). This represents a 4.23 molar

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excess of lithium catalyst per mole of reactant, which may or may not fall within “an amount of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions” of formula (I). Also, the product mixture is of an unspecified ratio, so the number of moles of double bonds being reduced cannot be determined. Thus, the “amount of 0.8 to 2.5 times the amount necessary for reducing the carbon-carbon double bond at the 4,5-positions” of formula (I) simply cannot be determined on the basis of the disclosure.

The purpose of the written description requirement is to ensure that the inventor had possession of the specific subject matter claimed as of the filing date of the application. As recognized by MPEP §2163:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.” *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 identifies factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

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Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.

The written description requirement of 35 U.S.C. §112 requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”) Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

CONCLUSION

Claims 1-24 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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